

WHAT IS CLAIMED IS:

1. A method for treating a metabotropic glutamate disorder, comprising administering to a subject in need thereof, an effective amount of at least one antagonist which modulates metabotropic glutamate receptor 2, metabotropic glutamate receptor 3, and metabotropic glutamate receptor 5, thereby treating the disorder.
2. A method for treating a metabotropic glutamate disorder, comprising administering to a subject in need thereof, an effective amount of at least one antagonist which modulates metabotropic glutamate receptor 2, and metabotropic glutamate receptor 5, thereby treating the disorder.
3. A method for treating a metabotropic glutamate disorder, comprising administering to a subject in need thereof an effective amount of at least one antagonist which modulates metabotropic glutamate receptor 3 and metabotropic glutamate receptor 5, thereby treating the disorder.
4. The method of any one of claims 1 to 3, wherein the disorder is an addictive disorder.
5. The method of claim 4, wherein the addictive disorder is nicotine addiction, alcohol addiction, opiate addiction, amphetamine addiction, methamphetamine addiction, or cocaine addiction.
6. The method of claim 4, wherein the addictive disorder is nicotine addiction.
7. The method of claim 4, wherein the addictive disorder is cocaine addiction.
8. The method of any one of claims 1 to 3, wherein the disorder is depression.
9. The method according to claim 1, wherein the antagonist is 2-methyl-6-(phenylethynyl)-pyridine.
10. A combination comprising (a) at least one active ingredient selected from a metabotropic glutamate receptor 2 antagonist and a metabotropic glutamate receptor 3 antagonist, and

(b) at least one metabotropic glutamate receptor 5 antagonist, in which the active ingredients are present in each case in free form or in the form of a pharmaceutically acceptable salt, and optionally at least one pharmaceutically acceptable carrier; for simultaneous, separate or sequential use.

11. A combination comprising (a) at least one active ingredient which exhibits antagonistic activity against the metabotropic glutamate receptor 2 and the metabotropic glutamate receptor 3, and (b) at least one metabotropic glutamate receptor 5 antagonist, in which the active ingredients are present in each case in free form or in the form of a pharmaceutically acceptable salt, and optionally at least one pharmaceutically acceptable carrier; for simultaneous, separate or sequential use.

12. A combination comprising (a) at least one metabotropic glutamate receptor 2 antagonist, and (b) at least one active ingredient which exhibits antagonistic activity against the metabotropic glutamate receptor 3 and the metabotropic glutamate receptor 5, in which the active ingredients are present in each case in free form or in the form of a pharmaceutically acceptable salt, and optionally at least one pharmaceutically acceptable carrier; for simultaneous, separate or sequential use.

13. A combination comprising (a) at least one metabotropic glutamate receptor 3 antagonist, and (b) at least one active ingredient which exhibits antagonistic activity against the metabotropic glutamate receptor 2 and the metabotropic glutamate receptor 5, in which the active ingredients are present in each case in free form or in the form of a pharmaceutically acceptable salt, and optionally at least one pharmaceutically acceptable carrier; for simultaneous, separate or sequential use.

14. Combination according to any one of claims 10 to 13 which is a combined preparation or a pharmaceutical composition.

15. Combination according to any one of claims 10 to 13 for simultaneous, separate or sequential use in the treatment of an addictive disorder or depression.

16. Method of treating a warm-blooded animal having an addictive disorder or depression comprising administering to the animal a combination according to any one of claims 10

to 13 in a quantity which is jointly therapeutically effective against an addictive disorder or depression and in which the compounds can also be present in the form of their pharmaceutically acceptable salts.

17. A pharmaceutical composition comprising a quantity, which is jointly therapeutically effective against an addictive disorder or depression, of a pharmaceutical combination according to any one of claims 10 to 13 and at least one pharmaceutically acceptable carrier.
18. Use of a combination according to any one of claims 10 to 13 for the preparation of a medicament for the treatment of an addictive disorder or depression.
19. A commercial package comprising a combination according to any one of claim 10 to 13 together with instructions for simultaneous, separate or sequential use thereof in the treatment of an addictive disorder or depression.
20. A method for treating substance abuse, comprising administering to a subject in need thereof, an effective amount of at least one antagonist which modulates mGluR2, mGluR3, and mGluR5, or a combination according to any one of claims 10 to 13, wherein the effective amount is sufficient to diminish, inhibit or eliminate desire for and/or consumption of the substance in the subject.
21. The method of claim 20, wherein the substance is nicotine, alcohol, opiates, amphetamines, methamphetamines, or cocaine.
22. The method of claim 21, wherein LY341495 and 2-methyl-6-(phenylethynyl)-pyridine are administered to the subject.
23. A method of screening for an agent that improves the ability of a known inhibitor to at least partially normalize an intracranial self-stimulation (ICSS) threshold of a non-human mammalian subject, comprising:
 - a) affecting the ICSS threshold of the subject;
 - b) administering to the subject, a sufficient amount of the known inhibitor to at least partially normalize the ICSS threshold when administered alone or in combination with

another inhibitor, wherein the known inhibitor is an antagonist of at least one of mGluR2, mGluR3, and mGluR5;

- b) administering to the non-human mammalian subject, an effective amount of a test agent, wherein the test agent is a known or suspected antagonist of at least one of mGluR2, mGluR3, and mGluR5; and
- c) determining whether the test agent improves the ability of the known inhibitor to at least partially normalize the ICSS threshold, thereby identifying an agent that improves the ability of the known inhibitor to at least partially normalize ICSS threshold.

24. The method of claim 23, wherein the method identifies the test agent as an agent effective for the treatment of depression or an addictive disorder.

25. The method of claim 23, wherein the known inhibitor is LY341495 or 2-methyl-6-(phenylethynyl)-pyridine.

26. The method of claim 23, wherein the test agent improves the ability of the known inhibitor to inhibit desire for and/or consumption of an addictive substance.

27. A method for treating an addictive disorder, comprising:

- a) administering to a subject in need thereof, an effective amount of at least one antagonist that modulates at least one of mGluR2, 3, and 5 during a first time period, wherein the first time period is a time period wherein the subject expects to be in an environment wherein, or exposed to stimuli in the presence of which, the subject habitually uses an addictive substance; and
- b) administering at least one antagonist that modulates at least one of mGluR2 and/or 3 during a second time period, wherein the second time period is a time period wherein the subject is suffering from withdrawal and/or depression.

28. The method of claim 27, wherein one or both 2-methyl-6-(phenylethynyl)-pyridine and LY341495 are administered during the first time period, and LY341495 is administered during the second time period.

29. A method for treating depressive symptoms and anxiety symptoms of depression, comprising administering to a subject in need thereof, an effective amount of at least one

antagonist which modulates metabotropic glutamate receptor 2, metabotropic glutamate receptor 3, and metabotropic glutamate receptor 5, thereby treating the depressive symptoms and anxiety symptoms of depression.

30. The method of claim 29, wherein an antagonist of metabotropic glutamate receptor 2 and metabotropic glutamate receptor 3 is administered when the subject experiences depression symptoms, and an antagonist of metabotropic glutamate receptor 5 is administered when the subject experiences anxiety symptoms.
31. The method of claim 30, wherein LY341495 and 2-methyl-6-(phenylethynyl)-pyridine are administered to the subject.